

FIP UPDATE 2024

THE NUMBERS ARE IN, WHAT'S NEW & DR. SALLY COGGINS'S UPDATED TREATMENT PROTOCOLS



DR. SALLY COGGINS

FEBRUARY 2024

WHERE WERE WE? RECAP OF PREVIOUS AVAILABLE TREATMENT OPTIONS

- ✓ **GS44154**
 - Available in a tablet form. (BOVA)
- ✓ **Remdesivir**
 - Injectable.
 - Can be administered either SC or IV.
 - Is metabolised into GS441524.



WHAT HAVE WE LEARNT IN THE LAST YEAR?



THE SCIENCE

Research confirmed that Remdesivir is converted into GS441524 in cats, and that the **concentrations that are achieved are equivalent to that of straight GS441524.**

- Previous research had only demonstrated this in other species.

ORAL TREATMENT

Studies have confirmed efficacy of oral GS441524.

- Can be used **at the same dose rate** as the injectable formulations.
- **Achieves similar results** as injectable formulations.

DOSING

Previous thinking was that around 6mg/kg maintenance dosing was sufficient for non-neurological forms of the disease. We now know that **10mg/kg** should be the **minimum** maintenance dose (either injectable or oral).

- The reason for the change is that studies have shown that some cats on the lower dose came out of remission and needed a second course of treatment at a higher dose rate.



"Since we revised the dosages up, none of the subsequent cats that were recruited in the study have come out of remission."

- Dry form typically needs to stay on 15mg/kg

THE STATISTICS

- **Australians** have demonstrated **86% survival to six months.**
 - NB: If these cats **survived the first 48 hours, the survival rate is 96%.**
- **Overseas** studies, such as one conducted at the RVC (Green et al) have demonstrated **survival rates of 81.3%.**
- A retrospective study combining the Australian and UK data has shown survival rates of 84.4%.



WHAT HAVE WE LEARNT IN THE LAST YEAR? (CONT.)



"There is a lot of consistency in that we can expect survival rates upwards of 80% with these drugs, and the majority of these cats are dying in the first week of treatment, which I think is a space that needs further investigation."

NEW THERAPY

Mulnpiravir: potentially much cheaper.

UPDATED TREATMENT PROTOCOLS

"DEATH WEEK" – SURVIVING THE FIRST FEW DAYS OF THERAPY

REMEMBER: FIP is an **intensely inflammatory disease** and there is a **spectrum** in terms of severity and how affected each individual is.

Possible reasons why patients don't survive the first few days, and how we can get better at it:

- Treatment initiated **too late**.
 - Accessibility, or speed of access, to medications is a major reason for this.
 - Solution: Keep enough of it on the shelf to start therapy for the seriously ill patients if you can legally do this.
- Inadequate management of the ramifications of the **severe inflammatory cascade** associated with FIP, such as hypotension or DIC.
 - Admit them and manage them through the crisis, dealing with the effects of the disease. *E.g.* drain pleural effusions, manage hypotension and shock, while you initiate therapy.



CONSIDERATIONS FOR MANAGING THE NEWLY DIAGNOSED FIP CAT

- **Determine if the cat requires hospitalization:** For example, hospitalisation is required if they are not eating, have pleural effusions that need tapping, require ongoing monitoring or require IV fluids.
- **The very sick ones:**
 - Hospitalise
 - IV Remdesivir initially



"If they're at the level where I need to have them on a drip, then I'm going to be using IV Remdesivir for the first three to five days, until they start to turn that corner."



PRO-TIP: Order 2 bottles of Remdesivir to get them through the initial period, so owners don't need to commit to a full course of treatment in case they don't make it.

- **The not-so-sick ones (Still eating, euhydrated and comfortable)**
 - **Sent home on oral GS441524 tablets.**
 - One bottle of 50mg tablets (10 tablets) should get a 3kg cat through one week of treatment. (Dose rate of **10 - 15mg/kg.**)



NOTE: BOVA does now allow you to order bottles of 20 tablets, and you can bulk buy if needed which will save the owner money.



"You are usually going to know whether you're on the right track or not after one bottle."

UPDATED TREATMENT PROTOCOLS (CONT.)

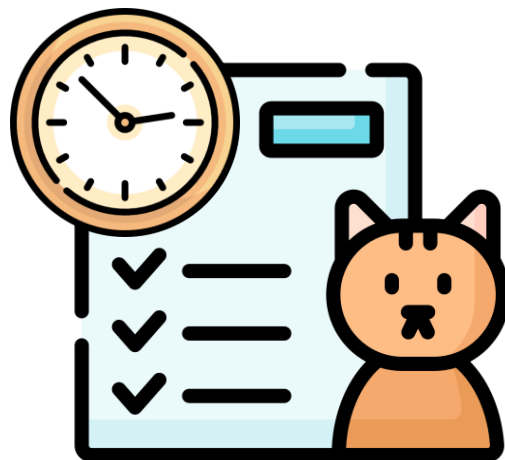
WHAT IF I'M NOT SURE IF MY PATIENT HAS FIP?

For cases where you are **highly suspicious of FIP** but you are unable to confirm the diagnosis (e.g. dry, neurologic or ocular forms) - consider a **treatment trial**.

- Commit to **5 days of treatment to see if you get a response**.

TREATMENT DURATION

As long as treatment is going well it is still recommended to **treat cats for 84 days, so 12 weeks of therapy**.



June 2023

Summary of current remdesivir / GS-441524 treatment protocols

Clinical presentation	Induction Day 0, 1, 2, 3	Maintenance Minimum 84 days total treatment
	Remdesivir Slow IV* or SC	Remdesivir SC OR GS-441524 PO^
Wet FIP(no neuro/ophthalmic)	10-15mg/kg q24h	10 mg/kg q24h
Dry FIP(no neuro/ophthalmic)	15mg/kg q24h	10 - 15mg/kg q24h
Ophthalmic involvement	15mg/kg q24h	12 - 15mg/kg q24h
Neurologic involvement	20mg/kg q24h	20mg/kg SC or 20 mg/kg as divided dose PO (e.g. 10mg/kg q 12hPO)

*Slow IV – Give as CRI over 20-30mins, can be diluted in saline

^PO – Give fasted with water bolus or tbsp wet food, full meal 30mins later

INJECTABLE VS. ORAL TREATMENT... IS ONE BETTER?

One treatment is more efficacious than the other, and the prices are pretty much identical.

REMEMBER: the injectable formulation has been known to cause significant injection site pain in **some** cats.

- After two weeks of injections, some cats (not all) become quite difficult for owners to inject at home.
- The **oral bioavailability of the tablets is excellent**, so they do not need to be on injectable treatment if the cat is able to be tableted.



"I'm happy with the efficacy of the tablets, versus the injection. So, I don't really see a need to be doing painful injections at home if they can tablet the cat successfully."



NOTE: Some owners may find it harder to tablet their cat than give a subcutaneous injection, so it depends on each individual case and how unwell they are initially.



COST UPDATE

(AUSTRALIAN DATA EARLY 2024 – BOVA, PRICES EXCL. GST)

Full course of registered treatment (BOVA)

- Approximately **\$3500 for a full course of treatment** (at cost-price) for a 3kg cat. (Heavier cat equals more \$\$)



First few days:

- Approximately \$99 per vial. (vs \$250 back in 2021)
 - 2 vials should get you through the initial treatment phase for an average sized cat.
- Bottle of oral GS (10 tabs) - approximately \$480, for 20 tabs \$795; (most cats are on 50mg), which will get you through the first 10 days.
- Update: GS is now also available as an oral liquid. 25 ml (50mg/ml) at \$790, which works out to about the same as the tablets.



NOTE: Once you know the cat is responding ordering in bulk will bring the price down.



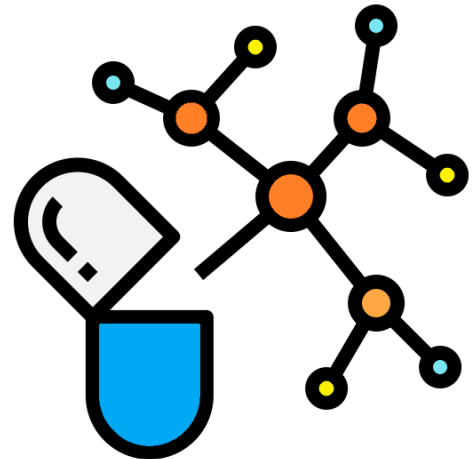
"It is definitely still a financial barrier for a lot of owners to go on to treatment. I do generally find if you can convince them just to start to see whether it's going to help, they tend to be able to find the cash to keep going once they see how much better their cat is."

BUT there is a cheaper option...

MOLNUIRAVIR

This is another pro-drug in the same family of nucleotide analogues as Remdesivir.

- Metabolised into EIDD1931.
- Preliminary data from Australia and overseas has shown that it is **relatively equivocal in its efficacy** to Remdesivir and GS441524.
- Used in some countries, including Australia, for COVID treatment.
 - Registered for GPs to prescribe it via a script from a pharmacy, which means that vets are also allowed to write a script for it. However, it is still quite expensive if obtained in this way.



How to obtain it cheaper in Australia?

- In Australia it can be obtained via an import permit through a 'Personal Access Scheme'. (<https://www.tga.gov.au/products/unapproved-therapeutic-goods/personal-importation-scheme>)
 - Works off the assumption that their pet cat is a 'family member' and allows owners to order human grade drugs through 'India Mart' which is a much cheaper supplier of medications.
 - For more details contact Dr Sally at sally.coggins@sydney.edu.au or Dr Richard Malik at richard.malik@sydney.edu.au

These medications are made on licence and are human grade, so not black-market formulations.

This allows the owner to obtain a whole course of treatment (i.e. the full 12 weeks) for less than \$100.

- It can however take some time for owners to get set up on the personal access scheme, so the cat may need to be started on Remdesivir or GS441524 tablets and then switched across.

MOLNUPIRAVIR (CONT.)



NOTE: It is completely fine to switch them straight onto Molnupiravir e.g. one day they get Remdesivir and the next they get Molnupiravir.



"Molnupiravir is amazing because it does now mean that in Australia, I don't think there's ever a case where it's going to be cost prohibitive to start them on treatment."

DOSING

Comes in 200mg capsules, which needs to be split and subdivided. Absorption not thought to be affected by food, so can give with food.

THE DOWNSIDES

CAUTION however...it doesn't appear to have the same safety margin as GS441524.

- There have been some cases of **bone marrow suppression causing neutropaenia** when it is being used at higher dose rates.
- Also reports of brittle whiskers, flaky skin, nausea, anorexia and muscle wasting, plus 'folder ear tips', although this may be disease-related.

Molnupiravir PRELIMINARY SUGGESTED use

Clinical presentation	Dosage molnupiravir PO
Minimum 84 days total treatment	
Wet FIP (no neuro/ophthalmic)	10 mg/kg q12h
Dry FIP (no neuro/ophthalmic)	12 mg/kg q12h
Ophthalmic involvement	12 - 15 mg/kg q12h
Neurologic involvement	15 mg/kg q12h

Do NOT exceed 15mg/kg q12h



"We can't just keep giving more if it's not working, whereas with GS441524, quite often we will escalate doses considerably higher than those maintenance doses. With Molnupiravir, we need to be a lot more judicious in terms of the actual dose that the animal's receiving."

Is there any preference in terms of what treatment to select?



"My preference is still GS441524. I do still think that that's the better and probably safer drug. So, if it's not cost prohibitive, keep them on GS441524 orally and I am still advocating for treating to 84 days, until we have more of those prospective results available."



One Health considerations:

There has been some evidence in humans treated for COVID that **resistance** to Molnupiravir develops more quickly than with Remdesivir.



"They're not completely comparable diseases and it's just something where future research needs to be focused, but I think we really do need to start looking for resistance surveillance."

GENERAL APPROACH TO TREATMENT AND DOSE RATES

DOES THE CAT NEED HOSPITALISATION OR NOT?

If **YES**: IV Remdesivir until it improves (usually 3 - 5 days).

- **Dose rate:**

- **Wet FIP** (without ophthalmic or neurologic involvement): **15mg/kg** for the first few days which can be **dropped to 10mg/kg for maintenance**.
- If on tablets, **round up to the nearest quarter** tablet which may mean they are on slightly higher than the 10mg/kg minimum.
- **Dry and ophthalmic FIP**: **15mg/kg** initially and then remain on this dose for maintenance.
- **Neurologic FIP**: Initial dose of **20mg/kg IV**. Then transition them to an **oral dose of 10mg/kg BID (20mg/kg/day)**.
 - Again, make sure you are **rounding up to the nearest quarter** tablet.



"Pretty much most cats end up on more than 10mg/kg by the time you're rounding with tablets."

REMEMBER: You need to consider '**weight creep**' which means you need to anticipate and account for the fact that these cats are going to put on weight between two-week weight checks as they clinically improve.

Minimum monitoring time points

Physical exam (Wt check) 2 weekly

Focus on clinical response in the first 6 weeks of treatment

CBC/Biochem at 6-8 weeks, then 10-12 weeks

If a dose increase is required, recheck 1-2 weeks after dose increase to ensure response

If dose extension is required, recheck 2 weekly until remission achieved



WHAT TO DO IF YOUR PATIENT IS NOT RESPONDING AS EXPECTED?

See JVIM for published data of expected days to normalisation of certain symptoms (e.g. normalisation of pyrexia, effusions, globulins). <https://onlinelibrary.wiley.com/doi/10.1111/jvim.16803>

ROUGH GUIDE:

- If still **pyrexia at 7 days** post treatment initiation, **increase the dose or change the drug**.
- If at **4 - 5 weeks of treatment the cat still has effusions**, this is a delayed response and the dose needs to be **increased by 5mg/kg** or consider changing the cat to a **different anti-viral** (e.g. Molnupiravir) and see if this makes a difference.



"We have definitely had instances where you go from one drug to the other and their symptoms respond considerably. There are some cats that are receiving GS441524 and Molnupiravir together and having improved outcomes."



When to consider a dose increase of remdesivir / GS-441524?

Pyrexia / inappetence	> 5-7 days
Effusions	> 2 weeks
WBC abnormalities	> 3 weeks
Tbil	> 3 weeks
Hyperglobulinaemia	> 6 - 8 weeks
Alb:glob < 0.6	> 8 - 10 weeks
Develop new signs referable to FIP at any stage in treatment	

Increase dose by 5 mg/kg (minimum 3 mg/kg)

